Imaging cancer heterogeneity and therapy resistance in real time

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A major challenge in biology and medicine is the ability to visualize and understand normal and diseased processes as they occur in vivo. To begin to address this, we have developed molecular strategies to image cell dynamics within cancers as they grow, progress, and recur in vivo. Based on our discovery that the stem cell determinant Musashi is reactivated in many cancers as they develop and progress, we created Msi1 and Msi2 knock-in reporter mice. In these mice, a fluorescent signal reflective of endogenous Msi expression allows high resolution visualization and tracking of Msi expressing cells. Using these unique tools together with high resolution real time imaging methods, we have found that a rise in Msi reporter activity marks the transition from benign lesions to a malignant aggressive state, and that Msi reporter activity uniquely marks tumor propagating capacity as well as therapy resistance in both hematologic malignancies and solid cancers. By providing a molecular view of the high-risk cells that drive cancer development and progression, our work has significant implications for developing new methods for early detection and targeted delivery of current therapies.